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Hepatitis E in South Africa: Evidence for Sporadic Spread and Increased Seroprevalence in Rural Areas

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Hepatitis E virus (HEV) is a major cause of non-A, non-B hepatitis in developing countries. Factors influencing sporadic spread of hepatitis E are unclear. We examined anti-HEV seroprevalence and demographic data from 407 urban and 360 rural black South African adults living in formal housing, squatter camps, or mud huts. Anti-HEV seroprevalence ranged from 5.8% to 19.1% (mean 10.7%) in the different regions. Mean urban and rural rates were 6.6% and 15.3%, respectively ($P = 0.0001$). Rural mud hut dwellers, using unchlorinated river water, were at greater risk (17.4%) than rural villagers (5.3%; $P = 0.008$). A linear relation was found between seroprevalence and age, suggesting sporadic spread. The high prevalence in mud hut dwellers suggests that contaminated water plays a major role in HEV spread in South Africa. Routine chlorination or boiling of river drinking water before consumption may reduce HEV infection.

KEY WORDS: HEV, viral hepatitis, South Africa, epidemiology

INTRODUCTION

The hepatitis E virus (HEV) is a major cause of non-A, non-B epidemic hepatitis and is acquired by the ingestion of contaminated water or food [Khuroo et al., 1983; Naik et al., 1992]. HEV is also spread sporadically [Hyams et al., 1992], but information on the mode of spread is unclear. No long-term carriers of HEV have been documented.

Adult anti-HEV seroprevalence rates of 4–11% have been reported in various developing countries [Lee et al., 1994; Thomas et al., 1993; Pujol et al., 1994]. HEV has been documented in South Africa [Robson et al., 1992; Grabow et al., 1994], but no data exist on the prevalence of anti-HEV in a representative sample of South African communities who are at greatest risk of acquiring the disease.

The aim of this study was to evaluate the seroprevalence of anti-HEV in rural and urban adult black South Africans living in the Western and Eastern Cape Provinces. The study was designed to allow differences in HEV exposure between rural and urban groups to be detected, to explore whether spread was epidemic or sporadic, and to identify factors associated with an increased risk of HEV infection.

MATERIALS AND METHODS

Patients and Sampling

This study was approved by the ethics committee of the Faculty of Medicine of the University of Cape Town. Consenting persons were recruited from both urban (Cape Town and Mdantsane) and rural (Keiskammahoek and Peddie) areas of South Africa. Urban samples included those from both the formal housing and the squatter communities; rural samples included people living in formal housing within villages as well as those living as subsistence farmers in isolated clusters of traditional mud huts. All recruits were resident in the relevant sample area for at least 5 years; 18 years and older, and ambulant. The initial sample was outpatient based. Six hundred seven persons were recruited in nonspecialist outpatient departments (OPD) of local hospitals, day hospitals, or clinics. Those recruited were sequential, consenting adults in the OPD queues of the relevant institutions. A separate community-based sample population of 160 persons was recruited in the rural district of Keiskammahoek. In the latter study, sampling regions within Keiskammahoek were randomly chosen by numbering the regions and choosing four by random number chart. Within these chosen regions, plots approximately half an acre in size (independent of the number of houses) were considered to be a sampling unit. Every second unit was sampled. Eligible, consenting occupants of each unit were numbered and at maximum two per-

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TABLE I. Regional Demographic Data Regarding Sample Number, Age, and Corresponding Prevalence of Anti-HEV

Region	Sample number	Age; mean (range)	Prevalence of anti-HEV (%)
Cape Town formal housing	135	40.8 (24–77)	8.2
Cape Town squatters	100	39.6 (23–72)	6
Mdantsane	172	37.8 (18–85)	5.8
Peddie	109	43 (18–83)	6.4
Keiskammahoek	251	47.3 (18–80)	19.1
Total	767	42.4 (18–85)	10.7

sons were randomly chosen (by random number chart) for inclusion.

Questionnaire

A questionnaire was completed for each person recruited. The questionnaire elicited details regarding the person's age, gender, house type, access to water, history of hepatitis, and known and putative risk factors for acquiring either enterally or parentally transmitted viral hepatitis.

Laboratory Methods

All blood samples were immediately separated and the sera stored at −20°C. Seroprevalence of anti-HEV and markers of hepatitis A, B, and C were determined. The HEV enzyme-linked immunosorbent assay (Abbott HEV EIA; Abbott Laboratories, North Chicago, IL) used two Burmese (Myanmar) strain recombinant antigens, representing sequences from open reading frames 2 and 3, for detection of antibodies to HEV. All samples were tested in duplicate and were repeated if indeterminate. Samples were considered true positives only when repeatedly reactive.

Antihepatitis A (HAV) IgG was assessed with the Abbott HAVAB-G radioimmunoassay (RIA; Abbott Laboratories; HBsAg was detected using the AUSRIA assay and anti-HBs with the AUSAB assay (Abbott Laboratories). Anti-HCV was determined by two second-generation EIAs (Ortho Diagnostics, Raritan, NJ and Behringwerke AG, Marburg, Germany) and considered positive only when reactive repeatedly. All tests were carried out according to the manufacturer's instructions.

Statistical Methods

Differences in prevalence were analysed using the χ^2 test. Discriminant analysis by stepwise method assessed factors associated with increased risk of infection. The linear model was used to estimate whether gradients differed significantly.

RESULTS

A cohort of 767 people was studied, of whom 407 (53%) were from urban areas and 360 (47%) from rural districts. Two hundred eighty (68.8%) urban dwellers lived in formal housing; the remainder were from squatter settlements. Seventy percent (252) of the rural group lived in traditional mud huts, with inadequate sewerage disposal and no access to chlorinated water. The average age of the entire sample was 42.4 years (range 18–85), and the male:female ratio was 1:1.8.

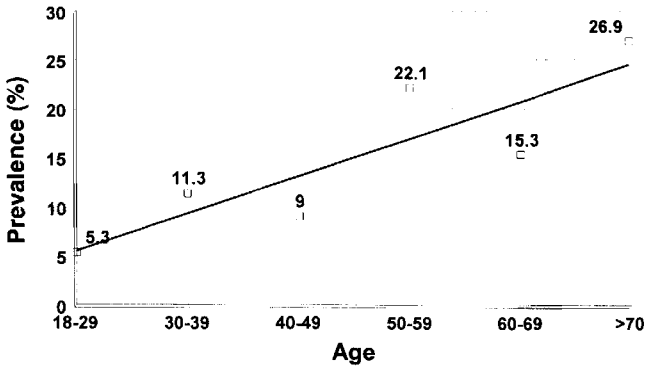

Fig. 1. Analysis by the f test (linear model) showed a linear association between age and seroprevalence of anti-HEV ($P < 0.05$).

Anti-HEV prevalence varied from 5.8% to 19.1% in the different regions, with mean urban and rural rates of 6.6% and 15.3%, respectively ($P = 0.0001$); see Table I). Rural persons living in mud huts had a significantly higher prevalence of anti-HEV than those living in the rural villages where water was chlorinated (17.4% vs. 5.3%; $P = 0.008$; odds ratio = 2.85). No differences were noted between the urban squatter and urban formal housing groups ($P > 0.05$).

Pit latrines were also shown to have an association with seropositivity ($P = 0.0013$); persons using toilets with water-borne sewerage were at a lower risk ($P = 0.0017$). Extremely few gave a history of hepatitis or any form of liver disease, suggesting a high degree of subclinical or low-grade hepatitis.

Discriminant analysis of all recruits showed rural location (0.364), age (0.589), living in mud houses (0.450), and lack of indoor plumbing (0.188) to be predictors of anti-HEV positivity (standardised coefficients in parentheses). Discriminant analysis of the rural group alone confirmed a greater risk for mud hut dwellers.

A linear relation was found between anti-HEV seroprevalence and age. When individual communities were examined, this relationship was maintained wherever sufficient positives allowed such analysis (see Fig. 1).

No differences in prevalence were found between the outpatient-based and community-based sampling. Sam-

TABLE II. Anti-HAV, HBsAg, HBsAb, and Anti-HCV Prevalences*

Region	Anti-HAV (%)	HBsAg (%)	HBsAb (%)	Anti-HCV (%)
Cape Town formal housing	97	4.4	55.6	3.7
Cape Town squatters	99	3	67	2
Mdantsane	98.8	4.7	61.6	0
Peddie	96.3	3.7	62.4	1.8
Keiskammahoek	97.8	5.5	58.2	2.2
Mean prevalence	97.9	4.3	60.8	1.8

*No significant differences were demonstrated between the regions for markers of HAV, HBV, or HCV infection.

TABLE III. Summary of Findings

Overall seroprevalence	10.7%
Seroprevalence range	5.8–19.1%
Rural vs. urban	15.3% vs. 6.6%
Rural town dwellers vs. rural mud hut dwellers	5.3% vs. 17.4%
Differences between urban squatters and formal housing residents	Nil

ples collected from the outpatient departments (79% of the total) were assessed for markers of hepatitis A, B, and C infection. The mean prevalences were anti-HAV 98%, HBsAg 4.3%, anti-HBs 61.1%, and anti-HCV 1.8%. No significant differences were shown between the different regions (see Table II).

DISCUSSION

Our data confirm a high prevalence of anti-HEV among adult black South Africans and show an increase in rural prevalence, which appears to be particularly marked in persons living in mud huts with no access to chlorinated water or adequate sewerage disposal (Table III). The prevalence of anti-HEV increased linearly with age, strongly suggesting that there has been no recent epidemic outbreak of HEV in the communities sampled and thus that infection is sporadic.

HAV and HEV are both transmitted by the faecal-oral route. However, their seroprevalence rates differed significantly in this study. Published data show that almost all black southern African children have been exposed to HAV early in life [Botha et al., 1994]. Although HEV infection has been shown in children [Hyams et al., 1992], infection is most commonly seen in adulthood [Dilawari et al., 1994]. Our data confirm that, unlike the case with HAV, many adults in developing countries remain susceptible to infection with HEV. The reasons for these discrepancies are currently unresolved but may lie in the high HEV titre required to cause infection.

The lack of difference in prevalence between the urban formal and urban squatter communities was surprising in view of the poor living conditions and the use of non-water-borne sewerage disposal methods within the majority of squatter areas. However, unlike their rural equivalents, who use river water, urban squatter communities rely entirely on chlorinated tap water for domestic use. Our data suggest that contaminated water plays a major role in the spread of HEV in South Africa and that home chlorination or boiling of drinking water might reduce infection with this virus.

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